

# PHARMACOLOGICAL REVIEWS

## *Editorial Board*

OTTO KRAYER, *Chairman*

HARRY EAGLE

ERIK JACOBSEN

U. S. v EULER

MARK NICKERSON

ALFRED GILMAN

DOUGLAS S. RIGGS

H. R. ING

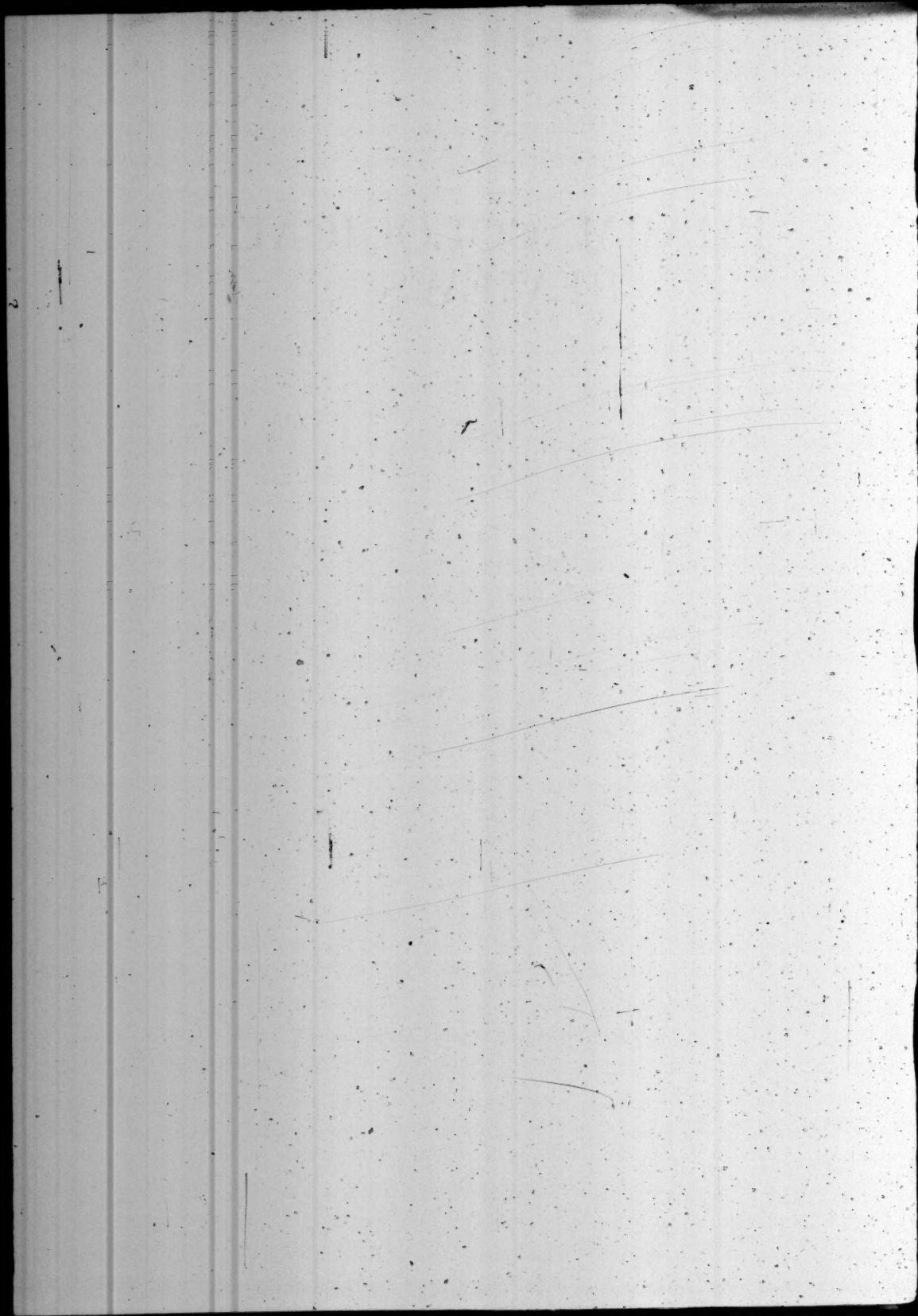
MARTHE VOGT

MILES WEATHERALL

VOLUME 7

1955

BALTIMORE, MARYLAND



## CONTENTS OF VOLUME 7

### NUMBER 1, MARCH 1955

|   |     |
|---|-----|
| Metabolism of the Mucopolysaccharides of Connective Tissue. ALBERT DORFMAN .....  | 1   |
| Motion Sickness. HERMAN I. CHINN AND PAUL K. SMITH .....  | 33  |
| Histochemistry—A Review. JONAS S. FRIEDENWALD .....   | 83  |
| Models for the Study of the Contraction of Muscle and of Cell Protoplasm. WILHELM<br>HASSELBACH AND ANNEMARIE WEBER ..... | 97  |
| Action of Drugs on Carotid Body and Sinus. C. HEYMANS .....   | 119 |

### NUMBER 2, JUNE 1955

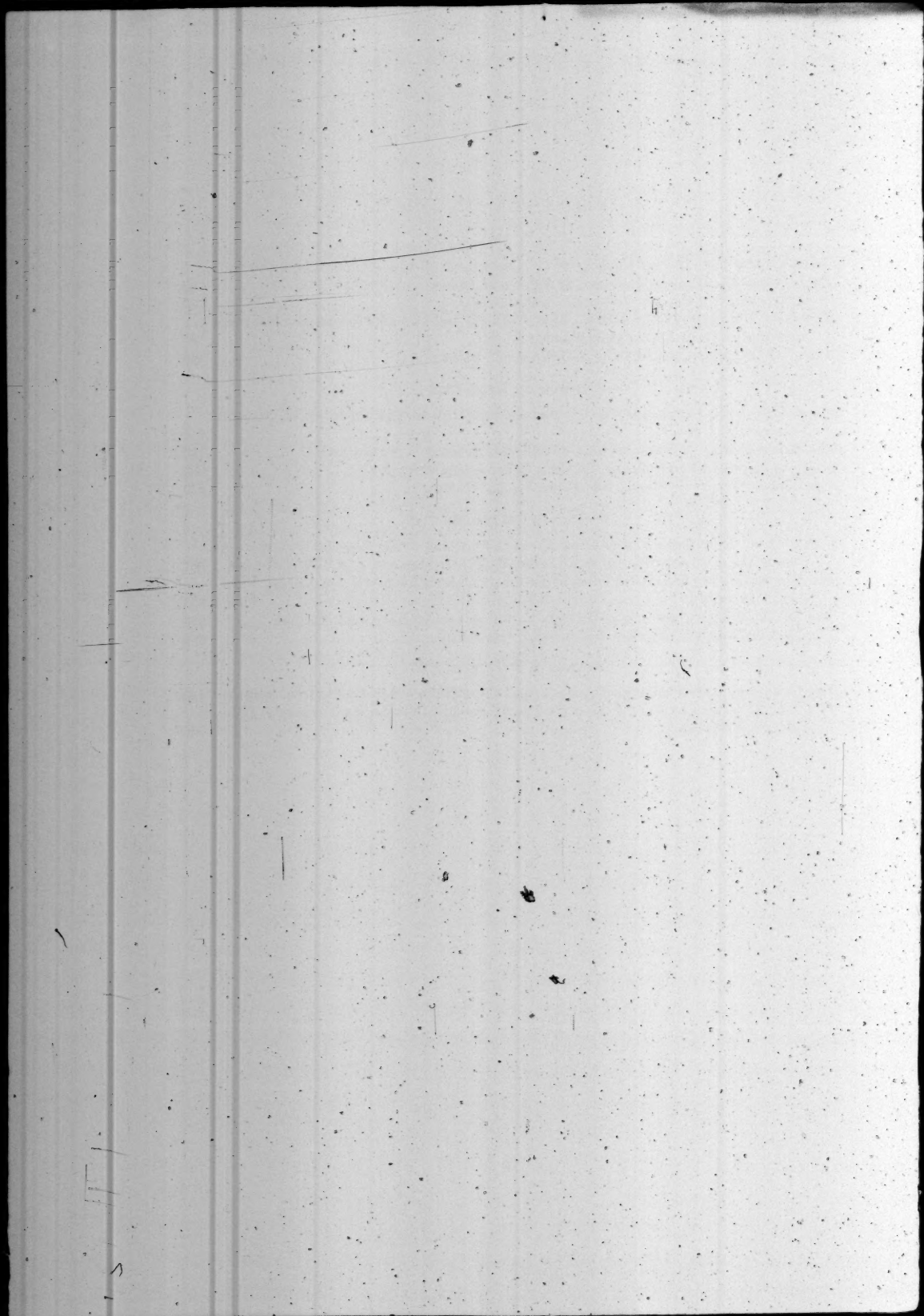
|  |     |
|--|-----|
| Physiological and Pharmacological Influences upon Intraocular Pressure. W. MORTON<br>GRANT ..... | 143 |
| The Pharmacology of Vascular Smooth Muscle. ROBERT F. FURCHGOTT .....                            | 183 |
| Pharmacology and Functions of the Mast Cells. JAMES F. RILEY .....                               | 267 |
| The Chemotherapy of Filarial Infections. FRANK HAWKING .....                                     | 279 |

### NUMBER 3, SEPTEMBER 1955

|   |     |
|---|-----|
| A Survey of the Factors Controlling Thyroid Function, with Especial Reference to<br>Newer Views on Antithyroid Substances. W. P. VANDERLAAN AND V. M. STORRIE ..... | 301 |
| The Uncoupling of Oxidative Phosphorylation as a Mechanism of Drug Action. THEO-<br>DORE M. BRODY .....   | 335 |
| The Pharmacology of Sweating. WALTER C. RANDALL AND KAZUO K. KIMURA .....   | 365 |
| The Metabolism and Toxicity of Methanol. OLUF RØE .....   | 399 |

### NUMBER 4, DECEMBER 1955

|   |     |
|---|-----|
| The Neurotoxins of <i>Clostridium botulinum</i> and <i>Clostridium tetani</i> . G. PAYLING WRIGHT .....       | 413 |
| The Use and Limitations of Atropine for Pharmacological Studies on Autonomic Effec-<br>tors. N. AMBACHE ..... | 467 |





## INDEX

- Acetylcholine, effect on vascular smooth muscle, 209
- local indirect vasoconstricting action, 246
- nicotinic and muscarinic actions, 371
- sweat gland response, 372
- Actomyosin, interactions with ATP, 98
- Adenosinediphosphate, *see* ADP
- Adenosinemonophosphate, *see* AMP
- Adenosinetriphosphate, *see* ATP
- Adenylic acid derivatives, effect on vascular smooth muscle, 209
- ADP, changes in concentration, influence on muscle contraction, 104
- Adrenal corticoids, sweat gland response, 390
- Alimentary tract muscles, effect of atropine, 470
- Alkali ions, role in muscle contraction, 108
- Ambache, N. Use and limitations of atropine for pharmacological studies on autonomic effectors, 467
- Amino group reagents, role in muscle contraction, 112
- Aminothiazole, incidence of toxic effects during clinical use, 324
- AMP, changes in concentration, influence on muscle contraction, 104
- Amyl nitrite, influence on intraocular pressure, 170
- Anesthetic, local, influence on intraocular pressure, 171
- Antagonism, irreversible competitive, kinetics of development of and recovery from, 223
- reversible competitive, kinetics of development of and recovery from, 218
- Antagonists, specific, effect on vascular smooth muscle, 211
- relative specificity, 225
- use in studies on vascular pharmacology and physiology, 226
- Antibiotics, role in uncoupling phosphorylation from oxidation, 346
- Antidromic phenomena, effect of atropine, 488
- Antihistamines, value in motion sickness, 61
- Antimoniais, action on filarial infections, 289
- Antithyroid agents, incidence of serious toxic effects and death during clinical use, 325
- substances, mode of action, 310
- Aqueous humor, inflow, 150
- outflow, 151
- rate of flow, determination by means of tracer substances, 162
- vessels containing, observations, 161
- Argemone oil, influence on intraocular pressure, 173
- Arsenicals, action on filarial infections, 291
- Atropine, effect on antidromic phenomena, 488
- on bladder muscles, 484
- on ganglia, 489
- on peristalsis, 475
- on response of motor neurones to nicotine stimulation, 475
- on response to vagal stimulation, species differences, 470
- on salivary glands, 486
- on skeletal muscle, 489
- resistance by nerve effect, 469
- response of muscular layers of intestine, 479
- susceptibility to, as criterion of cholinergic transmission, 469
- sweat gland response, 383
- use and limitations for pharmacological studies on autonomic effectors, 467
- value in classification of intestinomotor drugs, 483
- in motion sickness, 55
- ATP, changes in concentration, influence on muscle contraction, 102
- interactions with actomyosin, 98
- Azide, effect on vascular smooth muscle, 210
- Belladonna alkaloids, value in motion sickness, 64
- Binders, value in motion sickness, 52
- Bladder muscles, effect of atropine, 484
- Blocking agents, effects on vascular smooth muscle, 211
- Blood-aqueous humor barrier, estimation of permeability, 162
- Blood distribution, alterations, role in motion sickness, 49
- vessels, nature of terminal efferent innervation, 187
- orientation of muscle, 186

- Botulinum toxin, action on enzyme systems, 431  
   culture filtrates, presence of other "toxins," 424  
   evidence provided regarding neurology of intestine, 480  
   fixation and duration of action, 433  
   immunological types, 416  
   lethality for poikilothermic animals, 431  
   pathogenicity of different types for different animal species, 417  
   potentiation by serum and other materials, 423  
   purification, 421  
   resistance to heat and other agents, 420  
   site of action, 424  
 Botulism, action of anticholinesterase drugs; general features, 432  
 Brody, Théodore M. Uncoupling of oxidative phosphorylation as mechanism of drug action, 335  
 Caffeine, role in muscle contraction, 113  
 Calcium ion, role in muscle contraction, 106  
 Carbachol, sweat gland response, 381  
 Carbimazole, incidence of toxic effects during clinical use, 325  
 Cardiac glycosides, role in muscle contraction, 112  
 Carotid body chemoreceptors, pharmacological actions on, 123  
   physiological properties, 120  
 Carotid sinus pressoreceptors, action of drugs, 130  
 Cell metabolism, role of oxidative phosphorylation, 336  
   protoplasm, contraction, models for study, 97  
 Central nervous depressants, value in motion sickness, 58  
   depressing drugs, influence on intraocular pressure, 171  
   stimulating drugs, influence on intraocular pressure, 171  
 Cerebellum, role in motion sickness, 46  
 Cerebrum, role in motion sickness, 48  
 Chinn, Herman I. and Paul K. Smith. Motion sickness, 33  
 Chitosamine, *see* glucosamine  
 Chlorpromazine, value in motion sickness, 54  
 Cholinergic motor neurones, predominance in gut, supporting evidence, 481  
   transmission, susceptibility to atropine as criterion, 469  
 Chondrosamine, *see* Galactosamine  
*Clostridium botulinum*, neurotoxins, 413  
*tetani*, neurotoxins, 413  
 Cocaine, potentiating action, 236  
 Cyanine compounds, action on filarial infections, 292  
 Diamox, influence on intraocular pressure, 172  
 Dietary measures, value in motion sickness, 52  
 Diethylcarbamazine, clinical uses, 288  
   mode of action, 283  
   pharmacology and distribution, 287  
   relation of structure to activity, 283  
   toxicity, 286  
 Diffusible components, difficulties of localization in analysis *in situ*, 89  
 Diffusion of reaction product, problem in analysis *in situ*, 91  
 Diphenhydramine, value in motion sickness, 53  
 Dorfman, Albert. Metabolism of mucopolysaccharides of connective tissue, 1  
 Drugs for protection against motion sickness, methods of testing, 53  
 Electrical stimulation, role in uncoupling phosphorylation from oxidation, 355  
 Emetic trigger zone, role in motion sickness, 47  
 Enzyme localization, problem of possible diffusion in analysis *in situ*, 90  
   role in drug action, 335  
 Eosinophil, function in histamine problem, 272  
 Ephedrine, local indirect vasoconstricting action, 246  
   potentiating action, 238  
 Epinephrine, effect on vascular smooth muscle, 200  
   potentiation of responses to, possible source of error in studies, 233  
   sweat gland response, 386  
 Ethyl alcohol, effects on methanol poisoning, 404  
 Eye, cannulated, measurement, 159  
   gonioscopy, 163  
   intact, tonometry, 160  
   tonography, 160  
 5-Hydroxytryptamine, effect on vascular smooth muscle, 207  
   local indirect vasoconstricting action, 248

- Filarial infections, biology, 279  
chemotherapy, history, 282  
reaction to chemotherapy, 283
- Fixed tissue components, difficulties of localization in analysis *in situ*, 87
- Friedenwald, Jonas S. Histochemistry—a review, 83
- Furchgott, Robert F. Pharmacology of vascular smooth muscle, 183
- Furthrethonium, sweat gland response, 382
- Galactosamine, metabolism, 6
- Ganglia, effect of atropine, 489
- Ganglionic blocking drugs, influence on intraocular pressure, 170  
sweat gland response, 385
- Glaucoma, classification, 155  
pathogenesis, 155
- Glucosamine, metabolism, 6
- Glucuronic acid, metabolism, 3
- Grant, W. Morton. Physiologic and pharmacologic influences upon intraocular pressure, 143
- Graves' disease, value of antithyroid therapy, 314
- Ground substance, definitions, 2
- Halophenols, role in uncoupling phosphorylation from oxidation, 350
- Hasselbach, Wilhelm, and Annemarie Weber. Models for study of contraction of muscle and of cell protoplasm, 97
- Hawking, Frank. Chemotherapy of filarial infections, 279
- Heparin, location and function in mast cell, 270
- Heymans, C. Action of drugs on carotid body and sinus, 119
- Hexene-ol, sweat gland response, 382
- Hexosamines, metabolism, 6  
phosphorylation, 8
- Histamine, effect on vascular smooth muscle, 208  
influence on intraocular pressure, 170  
location and function in mast cell, 270
- Histochemistry, analysis *in situ* as method of approach, 87  
mechanical separation as method of approach, 84  
micro-dissection and micro-analysis as method of approach, 85  
review, 83
- Hormones, effects on metabolism of mucopolysaccharides, 22  
influence on intraocular pressure, 172
- Hyaluronidases, action, 12
- Hyoscine, value in motion sickness, 53
- Hypertension, effect on vascular smooth muscle, 207
- Hyperthyroidism, prognosis, influence of antithyroid substances, 326  
substances available for treatment, 315
- Hypnotic drugs, role in uncoupling phosphorylation from oxidation, 341
- Hypoxia, role in motion-sickness, 49
- Inosinetriphosphate, *see* ITP
- Intestine, muscular layers, response to atropine, 479  
neurology, contribution to understanding provided by botulinum toxin, 480
- Intestinomotor drugs, classification by means of atropine, 483
- Intraocular pressure, anatomic considerations, 146  
hydrodynamic considerations, 143  
influence of autonomic drugs, 164  
of drugs, methods for evaluating, 159  
of non-autonomic drugs, 170  
pathologic aspects, 154  
variation, 157  
pharmacologic influences, 164  
physiologic aspects, 150  
variations, 152
- Iodide ion, role in thyroid function, 302
- Iodothiouracil, incidence of toxic effects during clinical use, 324
- Isopropylarterenol, effect on vascular smooth muscle, 204
- ITP, changes in concentration, influence on muscle contraction, 104
- Kimura, Kazuo K., *see* Randall, 365
- Kinétosis, *see* Motion sickness
- Lergigan, value in motion sickness, 53
- Magnesium ion, role in muscle contraction, 105
- Mast cells, biological significance, 273  
morphology and distribution, 267  
pharmacology, 268
- Metal complexing agents, role in muscle contraction, 108
- Methacholine, sweat gland response, 381
- Methanol, absorption and distribution in organism, 399

- Methanol—Continued**  
 elimination by means of oxidation, 400  
   in expired air, 399  
 intoxication, hypotheses concerning  
   pathogenesis, 409  
   treatment, 405  
 lethal doses, 402  
 oxidation, mechanism, 401  
 metabolism, 399  
   poisoning, effects of ethyl alcohol, 404  
     pathological findings, 403  
     symptoms, 402  
   toxic doses, 402
- Methimazole**, incidence of toxic effects during clinical use, 321
- Methylthiouracil**, incidence of toxic effects during clinical use, 319
- Molecular mechanism of contraction**, substances and active groups of protein participating, 101
- "Monoamine oxidase hypothesis"** of potentiation of responses to epinephrine and norepinephrine by various drugs, 234
- Motion sickness**, drugs for protection,  
   value, 53  
   etiology, 41  
   incidence, 35  
   preventive drugs, action on cerebellum, 69  
     action on medulla, 70  
     undesirable side effects, 65  
     vestibular action, 68  
   prophylactic and therapeutic measures, 51  
   relationship to vestibular stimulation, 43  
   review of history, 33  
   role of central nervous pathway, 46  
     of non-labyrinthine stimuli, 48  
   selection of persons resistant, methods, 39  
   symptoms, 33
- Mucopolysaccharides**, biosynthesis in streptococci, 10  
   metabolism in mammals, 16  
   of connective tissue, metabolism, 1
- Muscle**, contraction, models for study, 97  
   *see also under* Vascular smooth muscle
- Nicotine**, local indirect vasoconstricting action, 246  
   stimulation, response of motor neurones,  
     effect of atropine, 475
- Sweat gland response**, 372
- Nitrates**, organic, effect on vascular smooth muscle, 210
- Nitrites**, effect on vascular smooth muscle, 210
- Nitrophenols**, role in uncoupling phosphorylation from oxidation, 350
- Norepinephrine**, effect on vascular smooth muscle, 203  
   potentiation of responses to, possible source of error in studies, 233
- Ocular hypotony**, nature of problem, 454
- Orthophosphate**, role in muscle contraction, 105
- Oxidative phosphorylation**, role in cell metabolism, 336
- Paraaminosalicylic acid**, antithyroid action, 310
- Parasympathetic blocking drugs**, sweat gland response, 383
- Parasympatholytic drugs**, influence on intraocular pressure, 166  
   value in motion sickness, 55
- Parasympathomimetic drugs**, influence on intraocular pressure, 164
- Peristalsis**, effect of atropine, 475
- Phenothiazine**, antithyroid action, 311
- Phenylbutazone**, antithyroid action, 311
- Phosphorylation uncoupling agents**, 341
- Physical therapy**, value in motion sickness, 52
- Physostigmine**, sweat gland response, 379
- Pilocarpine**, sweat gland response, 375
- Piperazine derivatives**, action on intestinal nematodes, 285
- Pitressin**, effect on vascular smooth muscle, 207
- Pituitary gland**, relationship to thyroid gland, 301
- Polyphosphates**, inorganic, role in muscle contraction, 104
- Propylthiouracil**, incidence of toxic effects during clinical use, 320
- Protein participating in molecular mechanism of contraction**, substances and active groups, 101
- Psychic factors**, role in motion sickness, 49
- Psychotherapy**, value in motion sickness, 52
- Quinine**, role in muscle contraction, 113
- Randall, Walter C., and Kazuo K. Kimura**. Pharmacology of sweating, 365



- Receptor hypothesis, development, 197  
theory for non-competitive antagonisms and "irreversible competitive antagonism," 214  
for "reversible competitive antagonism" and its application, 211
- Resorcinol, antithyroid action, 310
- R  c, Oluf. Metabolism and toxicity of methanol, 399
- Riley, James F. Pharmacology and functions of mast cells, 267
- Salicylates, role in uncoupling phosphorylation from oxidation, 349
- Salivary glands, effect of atropine, 486
- Sanguinarine, influence on intraocular pressure, 173
- Scopolamine, value in motion sickness, 55
- Skeletal muscle, effect of atropine, 489
- Smith, Paul K., *see* Chinn, 33
- Smooth muscle, *see under* Vascular smooth muscle
- Storrie, V. M., *see* VanderLaan, 301
- Sudorific agents, comparative effectiveness, 389
- Sulfhydryl reagents, role in muscle contraction, 109
- Sulfonic groups, substances containing, role in muscle contraction, 112
- Suramin, action on filarial infections, 293
- Sweat glands, response to various drugs, 372  
structure and function, 365  
sympathetic cholinergic innervation, 368
- Sweating experiments in animals and man, interpretation, 367
- Sympatholytic drugs, influence on intraocular pressure, 169
- Sympathomimetic amines, effect on vascular smooth muscle, 205  
local indirect vasoconstricting action, 246  
potentiating action, 238  
drugs, influence on intraocular pressure, 167
- Tachyphylactic phenomena, relation to local indirect vasoconstricting action of certain drugs, 249
- Temperature elevation, role in motion sickness, 49
- Tetanus, general features, 434  
toxin, lethality, effect of route of injection, 439  
lethality for poikilothermic animals, 454  
minimum lethal dose, difficulties in determination, 436<sup>+</sup>  
pathogenicity for various animal species, 438  
potentiation by serum and other agents, 437  
protection against, by prior injections of tetanus toxoid, 456  
purification, 435  
site of action, 440  
spread from depot site in tissues, 446
- Tetracycline drugs, antimicrobial activity, role of uncoupling, 348
- Thiobarbital, incidence of toxic effects during clinical use, 324
- Thiocyanate, role in thyroid function, 309
- Thiouracil, antithyroid function, 312
- Thiourea, incidence of toxic effects during clinical use, 323
- Thyroid gland, relationship to pituitary gland, 301  
hormone, role in thyroid function, 312  
role in uncoupling phosphorylation from oxidation, 352
- Tryptamine, local indirect vasoconstricting action, 248
- Tyramine, local indirect vasoconstricting action, 246
- Uncoupling, methods of studying, 337
- Urea, role in muscle contraction, 112
- Vagal stimulation, effect of atropine on response, species differences, 470
- VanderLaan, W. P., and V. M. Storrie. Survey of factors controlling thyroid function, with especial reference to newer views on antithyroid substances, 301
- Vascular smooth muscle, biochemistry, 195  
drug action, local potentiation, 229  
electrophysiology, 188  
local indirect action of certain drugs, 244  
responding to drugs, localization, 185  
response to changes in internal pressure, 193  
to electric stimulation, 193  
to light, 194  
to mechanical stimulation, 192  
to various drugs, 206  
tone, phasic variations, 189

- Vasoconstricting action of certain drugs, relation to tachyphylactic phenomena, 249
- Vestibular stimulation, relationship to motion sickness, 43
- Visceral displacement, role in motion sickness, 49
- Visual stimuli, role in motion sickness, 48
- Vitamins, value in motion sickness, 60
- Weber, Annemarie, *see* Hasselbach, 97
- Wright, G. Payling, Neurotoxins of *Clostridium botulinum* and *Clostridium tetani*, 413
- Wuchereria bancrofti*, eradication by diethylcarbamazine, 289
- malayi*, eradication by diethylcarbamazine, 289